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ABSTRACT

"REFRACTIVE CHANGES DURING PROLONGED EXPOSURE TO ALTITUDE FOLLOWING REFRACTIVE SURGERY" Christopher L. Blanton, M.D., Thomas Mader, M.D., Steven C. Schallhorn, M.D., John Ng, M.D., Benjamin Gilbert, M.D., Larry White, M.D.

Subject: Corneal changes in patients exposed to altitude after radial keratotomy and photorefractive keratectomy.

Purpose: to measure refractive parameters during exposure to altitude after radial keratotomy and photorefractive keratectomy.

Results: 6 radial keratotomy patients (11 eyes), 6 photorefractive keratectomy patients (12 eyes) and 9 control myopes (17 eyes) had the following measured at sea level: cycloplegic and manifest refraction, keratometry, and pachymetry both central and peripheral. Patients also had videokeratography performed prior to being taken to altitude. Subjects then had these same parameters measured daily at 14,110 feet on Pike's Peak, CO for 3 days. Radial keratotomy patients demonstrated a significant hyperopic shift and corneal flattening during exposure to altitude when compared to control myopic eyes. Patients who had undergone photorefractive keratectomy did not demonstrate a statistically significant shift in refraction or keratometry when compared with control myopes.

Significance: Anecdotal reports have shown hyperopic shifts in radial keratotomy patients after exposure to altitude. We confirmed this in a study population. Photorefractive keratectomy patients do not appear to be susceptible to this refractive shift.

INTRODUCTION

Radial keratotomy normally consists of four to sixteen deep radial incisions made in the mid-periphery of the cornea. These incisions cause the cornea to flatten centrally, thus decreasing myopia (a hyperopic shift). This procedure can currently be performed on active duty personnel not on flight or diving status. Excimer laser photorefractive keratectomy uses the Argon Fluoride (193 nm) laser to ablate and flatten the central cornea, thus also decreasing myopia. Some active duty personnel have undergone this excimer laser procedure as part of ongoing phase III FDA trials. Since military personnel are occasionally exposed to varying altitudes in unpressurized aircraft and during deployment, it is appropriate to investigate refractive changes that may take place with variations in altitude. A significant change in refractive error in military personnel deployed to varying altitudes could interfere with mission performance. Thus, it is extremely important that we document refractive changes with altitude following refractive surgery.

Radial keratotomy is a very commonly performed procedure for the correction of myopia. It is currently disqualifying for entry into the United States military, but may be performed on active duty personnel despite it being a disqualification for flight status and numerous special schools. Although many reports have described the post-operative stability of this procedure,[1,2] none have thus far documented stability of visual acuity at altitude. In a recent report we described changes in corneal shape and visual acuity observed in an ophthalmologist who traveled from sea level to 10,000 feet one year following a radial keratotomy.[3] He noted a pronounced change in visual acuity with this increase in altitude which suggests that refractive changes may be anticipated in individuals exposed to varying altitudes following radial keratotomy. Since a change in altitude of 10,000 feet or more is commonly achieved by deployed military personnel and aircraft crew members, such a change in refractive error is a potentially important aspect of radial keratotomy surgery which has not been previously explored. We recently performed a study on ten radial keratotomy patients by exposing them to simulated altitude to 12,000 feet in the altitude chamber at Ft. Rucker. Although we demonstrated a diurnal variation in refraction, corneal curvature and a trend toward decreased myopia, there was no statistically significant variation of these parameters caused by a six hour exposure to altitude. However, the previously quoted study subject had a documented change only after prolonged exposure (approximately 48 hours) to high altitude. There are currently no studies which evaluate the effect of prolonged exposure to altitude on excimer laser, either.

Small changes in corneal thickness are known to occur in normal corneas during sleep and as a result of local hypoxia brought about by contact lens use.[4] Although decreased ocular oxygen tension is well documented with increasing altitude,[5] the effect of hypoxia on the healthy cornea is rarely clinically significant. However, we hypothesize that when the normal corneal architecture is altered by radial incisions or laser treatment, the hypoxic cornea may be allowed to expand circumferentially. Endothelial cell damage which may occur near radial keratotomy incisions[7] could predispose this area to localized edema under hypoxic conditions. We hypothesize that even a small amount of corneal expansion near the radial keratotomy sites may cause circumferential elevation of the cornea peripheral to the optical zone. This annular band of corneal elevation may lead to central corneal flattening within the optical zone and a resultant hyperopic shift. The purpose of our study will be to determine if a statistically significant hyperopic shift in refractive error (0.75 diopters or more) occurs in subjects with radial keratotomies as compared to normals and patients who have undergone excimer photorefractive keratectomy during prolonged exposure to high altitude.

The military implications of this study are enormous. As stated previously, radial keratotomies can currently be performed on active duty personnel in the military excluding those on flight status. If significant changes in refractive error are noted to occur in subjects during our prolonged altitude study, this would suggest that any active duty soldiers who have had radial keratotomies may have visual acuity changes with altitude. Therefore the results of this study could have significant contribution to military preparedness.

MATERIALS AND METHODS

All patients who had undergone radial keratotomy at the Naval Medical Center in San Diego, and all patients who had undergone excimer laser photorefractive keratectomy as part of an IRB/FDA approved study at the Naval Medical Center in San Diego were invited to participate in this project. In addition, myopic control patients were recruited from the local active duty military personnel stationed at Naval Medical Center San Diego. All subjects had to be healthy, non-pregnant adults between the ages of 21-45 who had successful radial keratotomies or excimer laser photorefractive keratectomies for myopia. They must have had the surgical procedure approximately 4 months to 1 year prior to the study. All controls had to be healthy, non-pregnant adults between the ages of 21-45 with no previous history of ocular surgery. The following conditions were disqualifying:

a. any significant surgical complications at the time of surgery to include unplanned corneal incisions.
b. any postoperative complications to include infection or significant postoperative trauma.
c. any history of glaucoma or any ocular surgical procedure other than the radial keratotomy or excimer laser.
d. abnormal lid or facial anatomy which would prohibit adequate examination.
e. history of recent eye infection.
f. history of contact lens use within 6 months of this study.
g. positive pregnancy test

All individuals passed a complete physical, including: urinalysis, chest X-ray, VDRL, EKG, Blood Type, Hematocrit and Hemoglobin, cholesterol, triglycerides, fasting glucose, sickledex, HIV, Beta HCG (females) and complete dilated ocular exam.

We were able to recruit 6 radial keratotomy (RK) patients, 6 excimer photorefractive keratectomy (PRK) patients and 8 myopic control patients. All subjects underwent a detailed counseling session advising them of the risks of altitude exposure as part of their informed consent. We examined several ocular parameters at sea level including cycloplegic and manifest refraction, intraocular pressure, corneal keratometry, and corneal thickness, both central and peripheral. Patients also had computerized videokeratography performed.

Refractions were performed using a "push plus" technique with standard fogging. Cycloplegic refractions were performed 20 -30 minutes after two drops of tropicamide 1% spaced 5 minutes apart. Intraocular pressure was performed with the a calibrated tonopen™ (Biorad). All pressures were taken with the same instrument. Keratometry measurements were all performed on the same calibrated keratometer. Pachymetry was performed on a calibrated DGH ultrasonic pachymeter (DGH technologies, Farmington, PA). Pachymetry measurements were taken centrally, directly over the visual axis and peripherally at 12, 3, 6 and 9 o'clock. The peripheral measurements were all made half-way between the center of the cornea and the limbus. Finally all videokeratography was performed on the same calibrated EyeSys topography unit (Eyesys Laboratories, Houston, TX).

After these baseline examinations were performed patients were transferred the following day via commercial air to Colorado Springs, CO. The following day, the patients were transported to the summit of Pike's Peak where these same examinations were then performed for three consecutive days. Specifically, these patients were taken to the Pike's Peak Research Facility, a branch of the U.S. Army Research Institute of Environmental Medicine. The facility is located at an altitude of 14,110 feet above sea level. This altitude was chosen because military aircraft crew members may fly to this altitude without supplemental oxygen and troop deployment to this altitude is not uncommon. While being examined at altitude, oxygen saturation was monitored and recorded using a pulse oximeter. Patients were breathing ambient oxygen for the entire study. Barometric pressure was also recorded. After the exposure to altitude, the patients were returned to Colorado Springs, CO. The following day, all participants were once again returned to sea level. One week following their return to sea level, all subjects had their baseline examinations repeated. All examinations were performed between 9 and 12 A.M. in order to avoid diurnal shifts. Nineteen of the twenty patients had their pre-altitude exams performed in the local San Diego area One of the recruited radial keratotomy patients was from Tacoma, WA and so no pachymetry results were recorded for this patient during any of the exam periods.

Method of data analysis: Analysis of Variance with paired comparison tests for significant values was carried out using Bonferroni methodology.

1. The following parameters were evaluated and recorded on each subject:
    a. Cycloplegic and manifest refraction measured in diopters of sphere and cylinder and converted to spherical equivalent.
    b. Intraocular pressure
    c. Central and peripheral corneal thickness
    d. Corneal keratometry as measured in diopters

RESULTS

All refractive results will be given using the spherical equivalent. Examinations prior to altitude revealed the following. Manifest refraction in the radial keratotomy group was -0.45 D+/- 0.59. Cycloplegic refraction was -0.30 D +/- 0.65. The photorefractive keratectomy patients had a manifest refraction of 0.27 D +/- 0.62, with a similar cycloplegic refraction of 0.27 D +/- 0.54. Myopic controls had an average refractive error of -3.10 D +/- 1.01, and under cycloplegic conditions -3.07 D +/- 0.99. The average keratometric value for the radial keratotomy patients was 40.92 D +/- 1.14, PRK patients had a value of 40.36 D +/- 0.99, and myopic controls averaged 43.19 D +/- 0.53. Intraocular pressures were similar and in the mid-teens (table 1). Average central pachymetry results ranged from 530 for the PRK patients to 554 for the RK patients and 572 for the myopic control patients (table 1). Finally, peripheral pachymetry results were 616, 629, and 632 microns for the RK, PRK and myopic control groups respectively.

On day 1 at altitude, patients were re-examined. There was no statistically significant difference in any of the measured parameters when compared with the pre-altitude data On day 2 however, the radial keratotomy patients had experienced an hyperopic shift of 1.22 diopters (p= 0.009) when measured by manifest refraction. The cycloplegic refraction mimicked these results and a shift of 1.39 in the hyperopic direction was noted (p=0.001). The PRK patients and the control myopes experienced no statistically significant refractive changes either by manifest or cycloplegic refraction. A similar result was obtained on day 3 at altitude. Once again, the RK patients shifted in the hyperopic direction by both manifest and cycloplegic refraction. The average difference between day 3 at altitude and the pre-altitude exam was 1.52 diopters in the hyperopic direction by both manifest (p=0.000) and cycloplegic (p=0.000) refraction. PRK patients and control myopes once again showed no statistically significant shift in refraction. None of the post-altitude exams differed from the pre-altitude exams for any of the groups.

This same pattern was mimicked by keratometry measurements however, the differences did not reach statistical significance. Intraocular pressure measurements did not differ from pre-altitude values for any of the examinations in any of the groups. Central pachymetry measurements measured in the pre-altitude exam were different in all three groups. The average central pachymetry for control myopes was 572.24 +/- 22.33 microns. Radial keratotomy patients had an average central pachymetry of 554.67 +/- 23.40 microns and PRK patients demonstrated a central pachymetry of 530 +/- 25.0 microns. All three groups were different from each other when measured by analysis of variance. Within the control and PRK groups, there was no exam which differed from any other exam. In the RK group the exams on day 1 at altitude were different from days 2 and 3 at altitude. The central pachymetry thickened by an average 25.44 microns from day 1 to day 2 at altitude (p=0.039) and by 28.78 microns from day 1 to day 3 at altitude (p=0.013). No exams however differed from the pre-altitude examination. Peripheral pachymetry measurements did not differ amongst the three groups at the pre-altitude exam. All groups demonstrated corneal thickening which was statistically significant on days 2 and 3 at altitude. At the post-altitude exam, the corneal thickening had returned to baseline thickness.

DISCUSSION

The demonstration of hyperopic shifts in radial keratotomy patients when exposed to chronic altitude confirms what Mader has demonstrated anecdotally already in one radial keratotomy patient.[3] This raises many important issues related to not only active duty military patients but also to the population at large. The effect of hyperopic shifts in radial keratotomy patients is dependent upon the refractive error which has been achieved by the surgery. In patients who are under-corrected, the distance acuity may improve when exposed to altitude. In patients who are near emmetropia or over-corrected the hyperopic shift may decrease distance visual acuity. This is also dependent on the amount of shift which each individuals experience. Our range was from -0.25 to +3.125 diopters when measured by manifest refraction , and from -0.25 to 3.5 diopters by cycloplegic refraction. Although we demonstrated average shifts of approximately 1.25 -1.50 diopters after day 1, the value may need to be further refined in a larger more defined study population. For instance, the eleven radial keratotomy eyes in our study ranged from 4 to 31 months post-operative. This finding raises several more questions which need to be addressed in future studies. Is proximity to surgery a factor affecting the shift? Other questions include the evaluation of the effects of different altitudes. At what altitude, does this effect become important? Is there a threshold, or a gradual effect. Another obvious concern is the effect on near visual acuity. Patients may very well have debilitated reading vision. Once again, this is dependent upon the achieved refractive error, the patient's age and the amount of shift that an individual experiences.

Interestingly, the photorefractive patients appeared to have very stable refractive errors. The fact that photoablation only affects a relatively small percentage of the corneal depth when compared to the deep incisions required to achieve an effect in radial keratotomy may very well have a role in this difference. It certainly seems to offer an advantage over radial keratotomy in this respect.

Although we were unable to demonstrate a statistically significant difference when keratometry was examined, the trend and pattern were very similar and one could extrapolate these findings to theorize that with a larger study group, perhaps a difference could be demonstrated. Intraocular pressure did not appear to play a role as this parameter remained unchanged in all of the groups throughout the study.

Pachymetry readings revealed a difference in the pre-altitude exams with the PRK corneas being the thinnest and the control corneas being the thickest when central measurements were evaluated. Once again trends and patterns developed very similar to the refractive shifts. We were able to demonstrate a difference between the central thickness of the RK patients when day 1 at altitude was compared to days 2 and 3 at altitude. This finding may in part explain some of the refractive shifts demonstrated. Finally, the shifts in peripheral pachymetry demonstrated in all three groups suggest that hypoxic conditions at altitude caused subjects to experience decreases in endothelial pump metabolism. It may be that this decreased pump function may preferentially affect radial keratotomy patients causing them to experience hyperopic shifts when they are exposed to this metabolic stress at altitude.

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			TABLE 1		
	Pre-Altitude	Data			
	Manifest	Cyclo	Keratometry	IOP	Pach (C)
RK	-0.45	-0.30	40.92	14.82	554.67
STD	0.59	0.65	1.14	2.14	23.40
PRK	0.27	0.27	40.36	15.17	530.00
STD	0.62	0.54	0.99	3.13	25.00
Control	-3.10	-3.07	43.19	15.76	572.24
STD	1.01	0.99	0.53	2.99	22.33

Pach (P)
615.56
27.30
629.23
34.10
631.60
26.48